

GCTATAAGGA TCACGGCGCC CAGTCGACGC TGAGCTCCTC TGCTACTCAG AGTTGCAACC TCAGGCTCGCT

ATG GCT CCC AGC AGC CCC CGG CCC CTG CCC GCA CTC CTG GTC CTG GGG GCT CTG TTC CCA
 MET ALA PRO SER SER PRO ARG PRO ALA LEU PRO ALA LEU LEU VAL LEU LEU GLY ALA LEU PHE PRO

GGA CCT GGC AAT GCC CAG ACA TCT GTG TCC CCC TCA AAA GTC ATC CTG CCC CGG GGA GGC TCC GTG
 GLY PRO GLY ASN ALA GLN THR SER VAL SER PRO SER LYS VAL ILE LEU PRO ARG GLY GLY SER VAL

CTG GTG ACA TGC AGC ACC TCC TGT GAC CAG CCC AAG TTG GGC ATA GAG ACC CCG TTG CCT AAA
 LEU VAL THR CYS SER THR SER CYS ASP GLN PRO LYS LEU LEU GLY ILE GLU THR PRO LYS

AAG GAG TTG CTC CTG CCT GGG AAC AAC CCG AAG GTG TAT GAA CTG AGC AAT GTG CAA GAA GAT AGC
 LYS GLU LEU LEU LEU PRO GLY ASN ASN ARG LYS VAL TYR GLU LEU SER ASN VAL GLN GLU ASP SER

CAA CCA ATG TGC TAT TCA AAC TGC CCT GAT GGG CAG TCA ACA GCT AAA ACC TTC CTC ACC GTG TAC
 GLN PRO MET CYS TYR SER ASN CYS PRO ASP GLY GLN SER THR ALA LYS THR PHE LEU THR VAL TYR

TGG ACT CCA GAA CGG GTG GAA CTG GCA CCC CTC CCC TCT TGG CAG CCA GTG GGC AAG AAC CTT ACC
 TRP THR PRO PRO GLU ARG ARG VAL GLU LEU ALA PRO LEU PRO SER TRP GLN PRO VAL GLY LYS ASN LEU THR

CTA CGC TGC CAG GTG GAG GGT GGG GCA CCC CGG GCC AAC CTC ACC GTG CTG CTC CGT GGG GAG
 LEU ARG CYS GLN VAL VAL GLY GLY ALA PRO ARG ALA ASN LEU THR VAL VAL LEU ARG GLY GLU

AAG GAG CTG AAA CGG GAG CCA GCT GTG GGG GAG CCC GCT GAG GTC ACC ACC GTG CTG GTG AGG
 LYS GLU LEU LYS ARG GLU PRO ALA VAL GLY GLU PRO ALA GLU VAL THR THR VAL LEU VAL ARG

AGA GAT CAC CAT GGA GCC AAT TTC TGC CGC ACT GAA CTG GAC CTG CGG CCC CAA GGG CTG GAG
 ARG ASP HIS HIS GLY ALA ASN PHE SER CYS ARG THR GLU LEU ASP LEU ARG PRO GLN GLY LEU GLU

FIG. 1A

CTG TTT GAG AAC ACC TCG GCC CCC TAC CAG CTC CAG ACC TTT GTC CTG CCA GCG ACT CCC CCA CAA	CTG TTT GAG AAC ACC TCG GCC CCC TAC CAG CTC CAG ACC TTT GTC CTG CCA GCG ACT CCC CCA CAA
LEU PHE GLU ASN THR SER ALA PRO TYR GLN LEU GLN THR PHE VAL LEU PRO ALA THR PRO PRO GLN	LEU PHE GLU ASN THR SER ALA PRO TYR GLN LEU GLN THR PHE VAL LEU PRO ALA THR PRO PRO GLN
CTT GTC AGC CCC CCG GTC CTA GAG GTG GAC ACG CAG GGG ACC GTG GTC TGT TCC CTG GAC GGG CTG	CTT GTC AGC CCC CCG GTC CTA GAG GTG GAC ACG CAG GGG ACC GTG GTC TGT TCC CTG GAC GGG CTG
LEU VAL SER PRO ARG VAL LEU GLU VAL ASP THR GLN GLY THR VAL VAL CYS SER LEU ASP GLY LEU	LEU VAL SER PRO ARG VAL LEU GLU VAL ASP THR GLN GLY THR VAL VAL CYS SER LEU ASP GLY LEU
TTC CCA GTC TCG GAG GCC CAG GTC CAC CTG GCA CTG GGG GAC CAG AGG TTG AAC CCC ACA GTC ACC	TTC CCA GTC TCG GAG GCC CAG GTC CAC CTG GCA CTG GGG GAC CAG AGG TTG AAC CCC ACA GTC ACC
PHE PRO VAL SER GLU ALA GLN VAL HIS LEU ALA LEU GLY ASP GLN ARG LEU ASN PRO THR VAL THR	PHE PRO VAL SER GLU ALA GLN VAL HIS LEU ALA LEU GLY ASP GLN ARG LEU ASN PRO THR VAL THR
TAT GGC AAC GAC TCC TTC TCG GCC AAG GCC TCA GTC AGT GTG ACC GCA GAG GAC GAG GGC ACC CAG	TAT GGC AAC GAC TCC TTC TCG GCC AAG GCC TCA GTC AGT GTG ACC GCA GAG GAC GAG GGC ACC CAG
TYR GLY ASN ASP SER PHE SER ALA LYS ALA SER VAL SER VAL THR ALA GLU ASP GLU GLY THR GLN	TYR GLY ASN ASP SER PHE SER ALA LYS ALA SER VAL SER VAL THR ALA GLU ASP GLU GLY THR GLN
CGG CTG ACG TGT GCA GTA ATA CTG GGG AAC CAG AGC CAG GAG ACA CTG CAG ACA GTG ACC ATC TAC	CGG CTG ACG TGT GCA GTA ATA CTG GGG AAC CAG AGC CAG GAG ACA CTG CAG ACA GTG ACC ATC TAC
ARG LEU THR CYS ALA VAL ILE LEU GLY ASN GLN SER GLN GLU THR LEU GLN THR VAL THR ILE TYR	ARG LEU THR CYS ALA VAL ILE LEU GLY ASN GLN SER GLN GLU THR LEU GLN THR VAL THR ILE TYR
AGC TTT CCG GCG CCC AAC GTG ATT CTG ACG AAG CCA GAG GTC TCA GAA GCG ACC GAG GTG ACA GTG	AGC TTT CCG GCG CCC AAC GTG ATT CTG ACG AAG CCA GAG GTC TCA GAA GCG ACC GAG GTG ACA GTG
SER PHE PRO ALA PRO ASN VAL ILE LEU THR LYS PRO GLU VAL SER GLU GLY THR GLU VAL THR VAL	SER PHE PRO ALA PRO ASN VAL ILE LEU THR LYS PRO GLU VAL SER GLU GLY THR GLU VAL THR VAL
AAG TGT GAG GCC CAC CCT AGA GCC AAG GTG ACG CTG AAT GGG GTT CCA GCC CAG CCA CTG GGC CCG	AAG TGT GAG GCC CAC CCT AGA GCC AAG GTG ACG CTG AAT GGG GTT CCA GCC CAG CCA CTG GGC CCG
LYS CYS GLU ALA HIS PRO ARG ALA LYS VAL THR LEU ASN GLY VAL PRO ALA GLN PRO LEU GLY PRO	LYS CYS GLU ALA HIS PRO ARG ALA LYS VAL THR LEU ASN GLY VAL PRO ALA GLN PRO LEU GLY PRO
AGG GCC CAG CTC CTG CTG AAG GCC ACC CCA GAG GAC AAC GGG CCG AGC TTC TCC TCC TCT GCA ACC	AGG GCC CAG CTC CTG CTG AAG GCC ACC CCA GAG GAC AAC GGG CCG AGC TTC TCC TCC TCC TCT GCA ACC
ARG ALA GLN LEU LEU LEU LYS ALA THR PRO PRO GLU ASP ASN GLY ARG SER PHE SER CYS SER ALA THR	ARG ALA GLN LEU LEU LEU LYS ALA THR PRO PRO GLU ASP ASN GLY ARG SER PHE SER CYS SER ALA THR
CTG GAG GTG GCC GGC CAG CTT ATA CAC AAG AAC CAG ACC CCG GAG CTT CGT GTC TAT GGC CCC	CTG GAG GTG GCC GGC CAG CTT ATA CAC AAG AAC CAG ACC CCG GAG CTT CGT GTC TAT GGC CCC
LEU GLU VAL ALA GLY GLN LEU ILE HIS LYS ASN GLN THR ARG GLU LEU ARG VAL TYR GLY PRO	LEU GLU VAL ALA GLY GLN LEU ILE HIS LYS ASN GLN THR ARG GLU LEU ARG VAL TYR GLY PRO
CGA CTG GAC GAG AGG GAT TGT CCG GGA AAC TGG ACG TGG CCA GAA AAT TCC CAG CAG ACT CCA ATG	CGA CTG GAC GAG AGG GAT TGT CCG GGA AAC TGG ACG TGG CCA GAA AAT TCC CAG CAG ACT CCA ATG
ARG LEU ASP GLU ARG ASP CYS PRO GLY ASN TRP THR TRP PRO GLU ASN SER GLN THR PRO MET	ARG LEU ASP GLU ARG ASP CYS PRO GLY ASN TRP THR TRP PRO GLU ASN SER GLN THR PRO MET
TGC CAG GCT TGG GGG AAC CCA TTG CCC GAG CTC AAG TGT CTA AAG GAT GGC ACT TTC CCA CTG CCC	TGC CAG GCT TGG GGG AAC CCA TTG CCC GAG CTC AAG TGT CTA AAG GAT GGC ACT TTC CCA CTG CCC
CYS GLN ALA TRP GLY ASN PRO LEU PRO GLU LEU LYS CYS LEU LYS ASP GLY THR PHE PRO LEU PRO	CYS GLN ALA TRP GLY ASN PRO LEU PRO GLU LEU LYS CYS LEU LYS ASP GLY THR PHE PRO LEU PRO

FIG. 1B

ATC GGG GAA TCA GTG ACT GTC ACT CGA GAT CTT GAG GGC ACC TAC CTC TGT CGG GCC AGG AGC ACT
 ILE GLY GLU SER VAL THR VAL THR ARG ASP LEU GLU GLY THR TYR LEU CYS ARG ALA ARG SER THR

 CAA GGG GAG GTC ACC CGC GAG GTG ACC GTG AAT GTG CTC TCC CCC CGG TAT GAG ATT GTC ATC ATC
 GLN GLY GLU VAL THR ARG GLU VAL THR VAL ASN VAL LEU SER PRO ARG TYR GLU ILE VAL ILE ILE

 ACT GTG GTA GCA GCC GCA GTC ATA ATG GGC ACT GCA GGC CTC ACC AGC TAC CTC TAT AAC CGC CAG
 THR VAL VAL ALA ALA ALA VAL ILE MET GLY THR ALA GLY LEU SER THR TYR LEU TYR ASN ARG GLN

 CGG AAG ATC AAG AAA TAC AGA CTA CAA CAG GCC CAA AAA GGG ACC CCC ATG AAA CCG AAC ACA CAA
 ARG LYS ILE LYS LYS TYR ARG LEU GLN GLN ALA GLN LYS GLY THR PRO MET LYS PRO ASN THR GLN

 GCC ACG CCT CCC TGA ACCTATCCCG GGACAGGGCC TCTTCTCTCGG CCTTCCCATTA TTGGTGGCAG TGGTGCCACA
 ALA THR PRO PRO ***

 CTGAACAGAG TGAAGACAT ATGCCATGCA GCTACACCTA CCGGCCCTGG GAGCGCGGAG GACAGGGGCAT TGTCTCAGT

 CAGATACAAC AGCATTGGG GCCATGGTAC CTGCACACCT AAAACACTAG GCCACGCATC TGATCTGTAG TCACATGACT

 AAGCCAAGAG GAAGGAGCAA GACTCAAGAC ATGATTGATG GATGTTAAAG TCTAGCCTGA TGAGAGGGGA AGTGGTGGG

 GAGACATAGC CCCACCATGA GGACATACAA CTGGGAAATA CTGAAACTTG CTGCCTATTG GGTATGCTGA GGCCACAGA

 CTTACAGAAG AAGTGGCCCT CCATAGACAT GTGTAGCATC AAAACACAAA GGCCACACT TCCTGACGGA TGCCAGCTTG

 GGCACCTGCTG TCTACTGACC CCAACCCTTG ATGATATGTA TTTATTTCATT TGTTATTTTA CCAGCTATTT ATTGAGTGTC

 TTTTATGTAG GCTAAATGAA CATAGGTCTC TGGCCTCAGG GAGCTCCCAG TCCATGTCAC ATTCAGGTC ACCAGGTACA

 GTTGTAACAG TTGTACACTG CAGGAGAGTG CCTGGCAAAA AGATCAAAATG GGGCTGGGAC TTCTCATTTGG CCAACCTGCC

 TTTCCCCAGA AGGAGTGATT TTTCTATCGG CACAAAAGCA CTATATGGAC TGGTAATGGT TCACAGGTTT AGAGATTACC

FIG. 1C

CAGTGAGGCC TTATTCCTCC CTTCCCCCCA AACTGACAC CTTTGTAGC CACCTCCCCA CCCACATACA TTTCTGCCAG
 TGTTACAATG ACACTCAGCG GTCAATGTCTG GACATGAGTG CCCAGGGAAT ATGCCCAAGC TATGCCCTTGT CCTCTTGTCC
 TGTTTGCATT TCACTGGGAG CTTGCACAT TGCAGCTCCA GTTCTCTGCA GTGATCAGGG TCCTGCAAGC AGTGGGAAG
 GGGGCCAAGG TATTGGAGGA CTCCTCCCCA GCTTTGGAAG GGTCAATCCGC GTGTGTGTGT GTGTGTATGT GTAGACAAGC
 TCTCGCTCTG TCACCCAGGC TGGAGTGCAG TGGTGCAATC ATGGTCACT GCAGTCTTGA CCTTTTGGGC TCAAGTGATC
 CTCCCACCTC AGCCTCCTGA GTAGCTGGGA CCATAGGCTC ACAACACCCAC ACCTGGCAA TTTGATTTTT TTTTTTTTTT
 TCAGAGACGG GGTCTCGCAA CATTCCTTG ACTTCCTTG TGTAGTTAA TAAAGCTTTC TCAACTGCCA AAAAAAAAAA
 AAAAAA

FIG. 1D

FIG. 2A

TTCACATCAA AACTCCTATA CTGACCTGAG ACAGAGGCAG CAGTGATACC CACCTGAGAG ATCCTGTGTT TGA
 ACAACTG CTTCCCAAAA CGGAAAGTAT TTCAAGCCTA AACCTTTGGG TGAAGAAGAC TCTTGAAGTC ATG ATT
 met ile
 GCT TCA CAG TTT CTC TCA GCT CTC ACT TTG GTG CTT CTC ATT AAA GAG AGT GGA GCC TGG
 ala ser gln phe leu ser ala leu thr leu val leu leu ile lys glu ser gly ala trp
 TCT TAC AAC ACC TCC ACG GAA GCT ATG ACT TAT GAT GAG GCC AGT GCT TAT TGT CAG CAA
 ser tyr asn thr ser thr glu ala met thr tyr asp glu ala ser ala tyr cys gln gln
 AGG TAC ACA CAC CTG GTT GCA ATT CAA AAC AAA GAA GAG ATT GAG TAC CTA AAC TCC ATA
 arg tyr thr his leu val ala ile gln asn lys glu glu ile glu tyr leu asn ser ile
 TTG ACC TAT TCA CCA AGT TAT TAC TGG ATT GGA ATC AGA AAA GTC AAC AAT GTG TGG GTC
 leu ser tyr ser pro ser tyr tyr trp ile gly ile arg lys val asn asn val trp val
 TGG GTA GGA ACC CAG AAA CCT CTG ACA GAA GAA GCC AAG AAC TGG GCT CCA GGT GAA CCC
 trp val gly thr gln lys pro leu thr glu glu ala lys asn trp ala pro gly glu pro
 AAC AAT AGG CAA AAA GAT GAG GAC TGC GTG GAG ATC TAC ATC AAG AGA GAA AAA GAT GTG
 asn asn arg gln lys asp glu asp cys val glu ile tyr ile lys arg glu lys asp val
 GGC ATG TGG AAT GAT GAG AGG TGC AGC AAG AAG AAG CTT GCC CTA TGC TAC ACA GCT GCC
 gly met trp asn asp glu arg cys ser lys lys lys leu ala leu cys tyr thr ala ala
 TGT ACC AAT ACA TCC TGC AGT GGC CAC GGT GAA TGT GTA GAG ACC ATC AAT AAT TAC ACT
 cys thr asn thr ser cys ser gly his gly glu cys val glu thr ile asn asn tyr thr
 TGC AAG TGT GAC CCT GGC TTC AGT GGA CTC AAG TGT GAG CAA ATT GTG AAC TGT ACA GCC
 cys lys cys asp pro gly phe ser gly leu lys cys glu gln ile val asn cys thr ala

CTG GAA TCC CCT GAG CAT GGA AGC CTG GTT TGC AGT CAC CCA CTG GGA AAC TTC AGC TAC	leu glu ser pro glu his gly ser leu val cys ser his pro leu gly asn phe ser tyr
AAT TCT TCC TGC TCT ATC AGC TGT GAT AGG GGT TAC CTG CCA AGC AGC ATG GAG ACC ATG	asn ser ser cys ser ile ser cys asp arg gly tyr leu pro ser ser met glu thr met
CAG TGT ATG TCC TCT GGA GAA TGG AGT GCT CCT ATT CCA GCC TGC AAT GTG GTT GAG TGT	gln cys met ser ser gly glu trp ser ala pro ile pro ala cys asn val val glu cys
GAT GCT GTG ACA AAT CCA GCC AAT GGG TTC GTG GAA TGT TTC CAA AAC CCT GGA AGC TTC	asp ala val thr asn pro ala asn gly phe val glu cys phe gln asn pro gly ser phe
CCA TGG AAC ACA ACC TGT ACA TTT GAC TGT GAA GAA GGA TTT GAA CTA ATG GGA GCC CAG	pro trp asn thr thr cys thr phe asp cys glu glu gly phe glu leu met gly ala gln
AGC CTT CAG TGT ACC TCA TCT GGG AAT TGG GAC AAC GAG AAG CCA ACG TGT AAA GCT GTG	ser leu gln cys thr ser ser gly asn trp asp asn glu lys pro thr cys lys ala val
ACA TGC AGG GCC GTC CGC CAG CCT CAG AAT GGC TCT GTG AGG TGC AGC CAT TCC CCT GCT	thr cys arg ala val arg gln pro gln asn gly ser val arg cys ser his ser pro ala
GGA GAG TTC ACC TTC AAA TCA TCC TGC AAC TTC ACC TGT GAG GAA GGC TTC ATG TTG CAG	gly glu phe thr phe lys ser ser cys asn phe thr cys glu glu gly phe met leu gln
GGA CCA GCC CAG GTT GAA TGC ACC ACT CAA GGG CAG TGG ACA CAG CAA ATC CCA GTT TGT	gly pro ala gln val glu cys thr thr gln gly gln trp thr gln gln ile pro val cys
GAA GCT TTC CAG TGC ACA GCC TTG TCC AAC CCC GAG CGA GGC TAC ATG AAT TGT CTT CCT	glu ala phe gln cys thr ala leu ser asn pro glu arg gly tyr met asn cys leu pro

FIG. 2B

AGT GCT TCT GGC AGT TTC CGT TAT GGG TCC ACC AGC TGT GAG TTC TCC TGT GAG CAG GGT TTT	ser ala ser gly ser phe arg tyr gly ser ser ser cys phe ser cys glu gln gly phe
GTG TTG AAG GGA TCC AAA AGG CTC CAA TGT GGC CCC ACA GGG GAG TGG GAC AAC GAG AAG	val leu lys gly ser lys arg leu gln cys gly pro thr gly glu trp asp asn glu lys
CCC ACA TGT GAA GCT GTG AGA TGC GAT GCT GTC CAC CAG CCC CCG AAG GGT TTG GTG AGG	pro thr cys glu ala val arg cys asp ala val his gln pro pro lys gly leu val arg
TGT GCT CAT TCC CCT ATT GGA GAA TTC ACC TAC AAG TCC TCT TGT GCC TTC AGC TGT GAG	cys ala his ser pro ile gly glu phe thr tyr lys ser ser cys ala phe ser cys glu
GAG GGA TTT GAA TTA TAT GGA TCA ACT CAA CTT GAG TGC ACA TCT CAG GGA CAA TGG ACA	glu gly phe glu leu tyr gly ser thr gln leu glu cys thr ser gln gly gln trp thr
GAA GAG GTT CCT TCC TGC CAA GTG GTA AAA TGT TCA AGC CTG GCA GTT CCG GGA AAG ATC	glu glu val pro ser cys gln val val lys cys ser ser leu ala val pro pro gly lys ile
AAC ATG AGC TGC AGT GGC GAG CCC GTG TTT GGC ACT GTG TGC AAG TTC GCC TGT CCT GAA	asn met ser cys ser gly glu pro val phe gly thr val cys lys phe ala cys pro glu
GGA TGG ACG CTC AAT GGC TCT GCA GCT CGG ACA TGT GGA GCC ACA GGA CAC TGG TCT GGC	gly trp thr leu asn gly ser ala ala arg thr cys gly ala thr gly his trp ser gly
CTG CTA CCT ACC TGT GAA GCT CCC ACT GAG TCC AAC ATT CCC TTG GTA GCT GGA CTT TCT	leu leu pro thr cys glu ala pro thr glu ser asn ile pro leu val ala gly leu ser
GCT GCT GGA CTC TCC CTC CTG ACA TTA GCA CCA TTT CTC CTC TGG CTT CGG AAA TGC TTA	ala ala gly leu ser leu leu thr leu ala pro phe leu leu trp leu arg lys cys leu
CGG AAA GCA AAG AAA TTT GTT CCT GCC AGC AGC TGC CAA AGC CTT GAA TCA GAC GGA AGC	arg lys ala lys lys phe val pro ala ser ser cys gln ser leu glu ser asp gly ser

FIG. 2C

TAC CAA AAG CCT TCT TAC ATC CTT TAA GTTCAA AGAATCAGAA ACAGGTGCAT CTGGGGAAC T A
 tyr gln lys pro ser tyr ile leu ***
 GAGGGATAC ACTGAAGTTA ACAGAGACAG ATAACCTCTCC TCGGGTCTCT GGCCTTCTT GCCTACTATG CCAG
 ATGCCCT TTATGGCTGA AACCGCAACA CCCATCACCA CTTCAATAGA TCAAAAGTCCA GCAGGCAAGG ACGGCCT
 TCA ACTGAAAAGA CTCAGTGTTT CCTTTCCTAC TCTCAGGATC AAGAAAGTGT TGGCTAATGA AGGGAAGGA
 TATTTTCTTC CAAGCAAAGG TGAAGAGACC AAGACTCTGA AATCTCAGAA TTCCCTTTTCT AACTCTCCCT TG
 CTGGCTGT AAAATCTTGG CACAGAAACA CAATATTTG TGGCTTCTT TCTTTTGCC TCCACAGTGT TTCCA
 CAGCT GATTACACAG TTGCTGTCAT AAGAATGAAT AATAATTATC CAGAGTTTGA AGGAAAAAAA TGACTAAA
 AA TATTATAACT TAAAAAAATG ACAGATGTTG AATGCCCCACA GGCAATGCA TGGAGGGTTG TTAATGGTGC
 AAATCCTACT GAATGCTCTG TCGGAGGGTT ACTATGCACA ATTAAATCAG TTTCATCCCT ATGGGATTCA GTG
 CTCTTA AAGAGTTCTT AAGGATTGTG ATATTTTAC TTGCATTGAA TATATTATAA TCTTCCATAC TTCTTC
 ATTC AATACAAGTG TGGTAGGGAC TTAAAAAACT TGTAATGCT GTCAACTATG ATATGGTAAA AGTTACTTA
 T TCTAGATTAC CCCCTCATTT TTTATTAACA AATTATGTTA CATCTGTTT AAATTATTT CAAAAAGGA A
 ACTATTGTC CCTAGCAAG GCATGATGTT AACCAGAATA AAGTTCTGAG TGTCTTACT ACAGTTGTTT TTG
 AAAACA TGGTAGAATT GCAGAGTAAA AACTGAATGG AAGTTTGA TATTGTCAGA TATTTTTC GAAATAT
 GTG GTTCCACGA TGA AAAACTT CCATGAGGCC AAACGTTTTG AACTAATAAA AGCATAAATG CAAACACACA
 AAGGTATAAT TTTATGAATG TCTTTGTTGG AAAAGAATAC AGAAGATGG ATGTGCTTG CATTCCTACA AA
 GATGTTG TCAGATGTGA TATGTAAACA TAATTCTTGT ATATTATGGA AGATTTTAA TTCACAATAG AAAC T

CACCA TGTAAGAAGAG TCATCTGGTA GATTTTAAAC GAATGAAGAT GTCTAATAGT TATCCCTAT TTGTTTTC
 TT CTGTATGTTA GGGTGCTCTG GAAGAGAGGA ATGCTGTGT GAGCAAGCAT TTATGTTTAT TTATAAGCAG
 ATTTAACAAT TCCAAAGGAA TCTCCAGTTT TCAGTTGATC ACTGGCAATG AAAAATTCTC AGTCAGTAAT TGC
 CAAAGCT GCTCTAGCCT TGAGGAGTGT GAGAATCAAA ACTCTCCTAC ACTTCCATTA ACTTAGCATG TGTTGA
 AAAA AAAAGTTTCA GAGAAGTTCT GGCTGAACAC TGGCAACGAC AAAGCCACACA GTCAAAACAG AGATGTGAT
 A AGGATCAGAA CAGCAGAGGT TCTTTTAAAG GGCAGAAAA ACTCTGGGAA ATAAGAGAGA ACAACTACTG T
 GATCAGGCT ATGTATGGAA TACAGTGTTA TTTTCTTTGA AATTGTTTAA GTGTGTAA TATTTATGTA AACT
 GCATTA GAAATTAGCT GTGTGAATA CCAGTGTGT TTGTGTTTGA GTTTTATGA GAATTTTAAA TTATAAC
 TTA AAATATTTA TAAATTTTAA AGTATATATT TATTTAAGCT TATGTCAGAC CTATTGACA TAACACTATA
 AAGTTGACA ATAAATGTGC TTATGTTT

FIG. 2E

FIG. 3A

CGGGCCCTCAC TGGCTTCAGG AGCTGAATAC CCTCCAGGC ACACACAGGT GGGACACAAA TAAGGGTTTT GGA
 ACCACTA TTTTCTCATC ACGACAGCAA CTTAAA ATG CCT GGG AAG ATG GTC GTG ATC CTT GGA GCC
 met pro gly lys met val val ile leu gly ala
 TCA AAT ATA CTT TGG ATA ATG TTT GCA GCT TCT CAA GCT TTT AAA ATC GAG ACC ACC CCA
 ser asn ile leu trp ile met phe ala ala ser gln ala phe lys ile glu thr thr pro
 GAA TCT AGA TAT CTT GCT CAG ATT GGT GAC TCC GTC TCA TTG ACT TGC AGC ACC ACA GGC
 glu ser arg tyr leu ala gln ile gly asp ser val ser leu thr cys ser thr thr gly
 TGT GAG TCC CCA TTT TTC TCT TGG AGA ACC CAG ATA GAT AGT CCA CTG AAT GGG AAG GTG
 cys glu ser pro phe phe ser trp arg thr gln ile asp ser pro leu asn gly lys val
 ACG AAT GAG GGG ACC ACA TCT ACG CTG ACA ATG AAT CCT GTT AGT TTT GGG AAC GAA CAC
 thr asn glu gly thr thr ser thr leu thr met asn pro val ser phe gly asn glu his
 TCT TAC CTG TGC ACA GCA ACT TGT GAA TCT AGG AAA TTG GAA AAA GGA ATC CAG CTG GAG
 ser tyr leu cys thr ala thr cys glu ser arg lys leu glu lys gly ile gln val glu
 ATC TAC TCT TTT CCT AAG GAT CCA GAG ATT CAT TTG AGT GGC CCT CTG GAG GCT GGG AAG
 ile tyr ser phe pro lys asp pro glu ile his leu ser gly pro leu glu ala gly lys
 CCG ATC ACA GTC AAG TGT TCA GTT GCT GAT GTA TAC CCA TTT GAC AGG CTG GAG ATA GAC
 pro ile thr val lys cys ser val ala asp val tyr pro phe asp arg leu glu ile asp
 TTA CTG AAA GGA GAT CAT CTC ATG AAG AGT CAG GAA TTT CTG GAG GAT GCA GAC AGG AAG
 leu leu lys gly asp his leu met lys ser gln glu phe leu glu asp ala asp arg lys
 TCC CTG GAA ACC AAG AGT TTG GAA GTA ACC TTT ACT CCT GTC ATT GAG GAT ATT GGA AAA
 ser leu glu thr lys ser leu glu val thr phe thr pro val ile glu asp ile gly lys
 GTT CTT GTT TGC CGA GCT AAA TTA CAC ATT GAT GAA ATG GAT TCT GTG CCC ACA GTA AGG
 val leu val cys arg ala lys leu his ile asp glu met asp ser val val pro thr val arg

CAG GCT GTA AAA GAA TTG CAA GTC TAC ATA TCA CCC AAG AAT ACA GTT ATT TCT GTG AAT
 gln ala val lys glu leu gln val tyr ile ser pro lys asn thr val ile ser val asn
 CCA TCC ACA AAG CTG CAA GAA GGT GGC TCT GTG ACC ATG ACC TGT TCC AGC GAG GGT CTA
 pro ser thr lys leu gln glu gly gly ser val thr met thr cys ser ser glu gly leu
 CCA GCT CCA GAG ATT TTC TCG AGT AAG AAA TTA GAT AAT GGG AAT CTA CAG CAC CTT TCT
 pro ala pro glu ile phe trp ser lys lys leu asp asn gly asn leu gln his leu ser
 GGA AAT GCA ACT CTC ACC TTA ATT GCT ATG AGG ATG GAA GAT TCT GGA ATT TAT GTG TGT
 gly asn ala thr leu thr leu ile ala met arg met glu asp ser gly ile tyr val cys
 GAA GGA GTT AAT TTG ATT GGG AAA AAC AGA AAA GAG GTG GAA TTA ATT GTT CAA GCA TTC
 glu gly val asn leu ile gly lys asn arg lys glu val glu leu ile val gln ala phe
 CCT AGA GAT CCA GAA ATC GAG ATG AGT GGT GGC CTC GTG AAT GGG AGC TCT GTC ACT GTA
 pro arg asp pro glu ile glu met ser gly gly leu val asn gly ser val thr val
 AGC TGC AAG GTT CCT AGC GTG TAC CCC CTT GAC CGG CTG GAG ATT GAA TTA CTT AAG GGG
 ser cys lys val pro ser val tyr pro leu asp arg leu glu ile glu leu lys gly
 GAG ACT ATT CTG GAG AAT ATA GAG TTT TTG GAG GAT ACG GAT ATG AAA TCT CTA GAG AAC
 glu thr ile leu glu asn ile glu phe pro thr ile glu asp thr asp met lys ser leu glu asn
 AAA AGT TTG GAA ATG ACC TTC ATC CCT ACC ATT GAA GAT ACT GCA AAA GCT CTT GTT TGT
 lys ser leu glu met thr phe phe pro thr ile glu asp thr gly lys ala leu val cys
 CAG GCT AAG TTA CAT ATT GAT GAC ATG GAA TTC GAA CCC AAA CAA AGG CAG AGT ACG CAA
 gln ala lys leu his ile asp asp met glu phe glu pro lys gln arg gln ser thr gln
 ACA CTT TAT GTC AAT GTT GCC CCC AGA GAT ACA ACC GTC TTG CTC AGC CCT TCC TCC ATC
 thr leu tyr val asn val ala pro arg asp thr thr val leu val ser pro ser ile
 CTG GAG GAA GGC AGT TCT GTG AAT ATG ACA TGC TTG AGC CAG GGC TTT CCT GCT CCG AAA
 leu glu glu gly ser val asn met thr cys leu ser gln gly phe pro ala pro lys

ATC	CTG	TGG	AGC	AGG	CAG	CTC	CCT	AAC	GGG	GAG	CTA	CAG	CCT	CTT	TCT	TCT	GAG	AAT	GCA	ACT
ile	leu	trp	ser	arg	gln	leu	pro	asn	gly	glu	leu	gln	pro	leu	ser	glu	asn	ala	thr	
CTC	ACC	TTA	ATT	TCT	ACA	AAA	ATG	GAA	GAT	TCT	GGG	GTT	TAT	TTA	TGT	GAA	GGA	ATT	AAC	
leu	thr	leu	ile	ser	thr	lys	met	glu	asp	ser	gly	val	tyr	leu	cys	glu	gly	ile	asn	
CAG	GCT	CGA	AGA	AGC	AGA	AAG	GAA	GTG	GAA	TTA	ATT	ATC	CAA	GTT	ACT	CCA	AAA	GAC	ATA	
gln	ala	gly	arg	ser	arg	lys	glu	val	glu	leu	ile	ile	gln	val	thr	pro	lys	asp	ile	
AAA	CTT	ACA	GCT	TTT	CCT	TCT	GAG	ACT	GTC	AAA	GAA	GGA	GAC	ACT	GTC	ATC	ATC	TCT	TGT	
lys	leu	thr	ala	phe	pro	ser	glu	ser	val	lys	glu	gly	asp	thr	val	ile	ile	ser	cys	
ACA	TGT	CGA	AAT	GTT	CCA	GAA	ACA	TGG	ATA	ATC	CTG	AAG	AAA	AAA	GCG	GAG	ACA	GGA	GAC	
thr	cys	gly	asn	val	pro	glu	thr	trp	ile	ile	leu	lys	lys	ala	glu	thr	gly	asp		
ACA	GTA	CTA	AAA	TCT	ATA	GAT	GGC	CCC	TAT	ACC	ATC	CGA	AAG	GCC	CAG	TTG	AAG	GAT	CGC	
thr	val	leu	lys	ser	ile	asp	gly	ala	tyr	thr	ile	arg	lys	ala	gln	leu	lys	asp	ala	
GGA	GTA	TAT	GAA	TGT	GAA	TCT	AAA	AAC	AAA	GTT	GGC	TCA	CAA	TTA	AGA	AGT	TTA	ACA	CTT	
gly	val	tyr	glu	cys	glu	ser	lys	asn	lys	val	gly	ser	gln	leu	arg	ser	leu	thr	leu	
GAT	GTT	CAA	GGA	AGA	GAA	AAC	AAC	AAA	GAC	TAT	TTT	TCT	CCT	GAG	CTT	CTC	GTG	CTC	TAT	
asp	val	gln	gly	arg	glu	asn	asn	lys	asp	tyr	phe	ser	pro	glu	leu	val	leu	tyr		
TTT	GCA	TCC	TCC	TTA	ATA	ATA	CCT	CCC	ATT	GGA	ATG	ATA	ATT	TAC	TTT	GCA	AGA	AAA	CCC	
phe	ala	ser	ser	leu	ile	ile	pro	ala	ile	gly	met	ile	ile	tyr	phe	ala	arg	lys	ala	
AAC	ATG	AAG	GGG	TCA	TAT	AGT	CTT	GTA	GAA	GCA	CAG	AAA	TCA	AAA	GTG	TAG	CTA	ATG	CTTG	
asn	met	lys	gly	ser	tyr	ser	leu	val	glu	ala	gln	lys	ser	lys	val	***				

ATATGTTCAA CTGGAGACAC TATTATCTG TGCAAATCCT TGATACTGCT CATCATTCCT TGAGAAAC AAT

GAGCTGA GAGGCAGACT TCCCTGAATG TATTGAAGTT GGAAGAAAT GCCATCTAT GTCCCTTGCT GTGAGC

AAGA AGTCAAAGTA AAAGTTGCTG CCTGAAGAAC AGTAACTGCC ATCAAGATGA GAGAACTGGA GGAGTTTCCT

T GATCTGTATA TACAATAACA TAAATTGTAC ATATGTA AAA TAAAAATTATG CCATAGCAAG ATTGCTTAAAA

TAGCAACAC TCTATATTTA GATTGTTAAA ATAACTAGTG TTGCTTGGAC TATTATAATT TAATGCATGT TAGG
 AAAATT TCACATTAAAT ATTGCTGAC AGCTGACCTT TGTCTCTTTT CTTCATTTTT ATTCCCTTTC ACAAAT
 TTT ATTCTATAT AGTTTATTGA CAATAATTTC AGGTTTGTG AAGATGCCGG GTTTTATATT TTTATAGACA
 AATAATAAGC AAAGGGAGCA CTGGGTTGAC TTTCAGGTAC TAAATACCTC AACCTATGGT ATAATGGTTG AC
 TGGGTTTC TCTGTATAGT ACTGGCATGG TACGGAGATG TTTCACGAAG TTTGTTTCATC AGACTCCTGT GCAAC
 TTTC CAATGTGGCC TAAAAATGCA ACTTCTTTTT ATTTCTTTTT GTAAATGTTT AGTTTTTTTT GTATAGTA
 AA GTGATAAATT CTGGAATTAA AAA

FIG. 3D

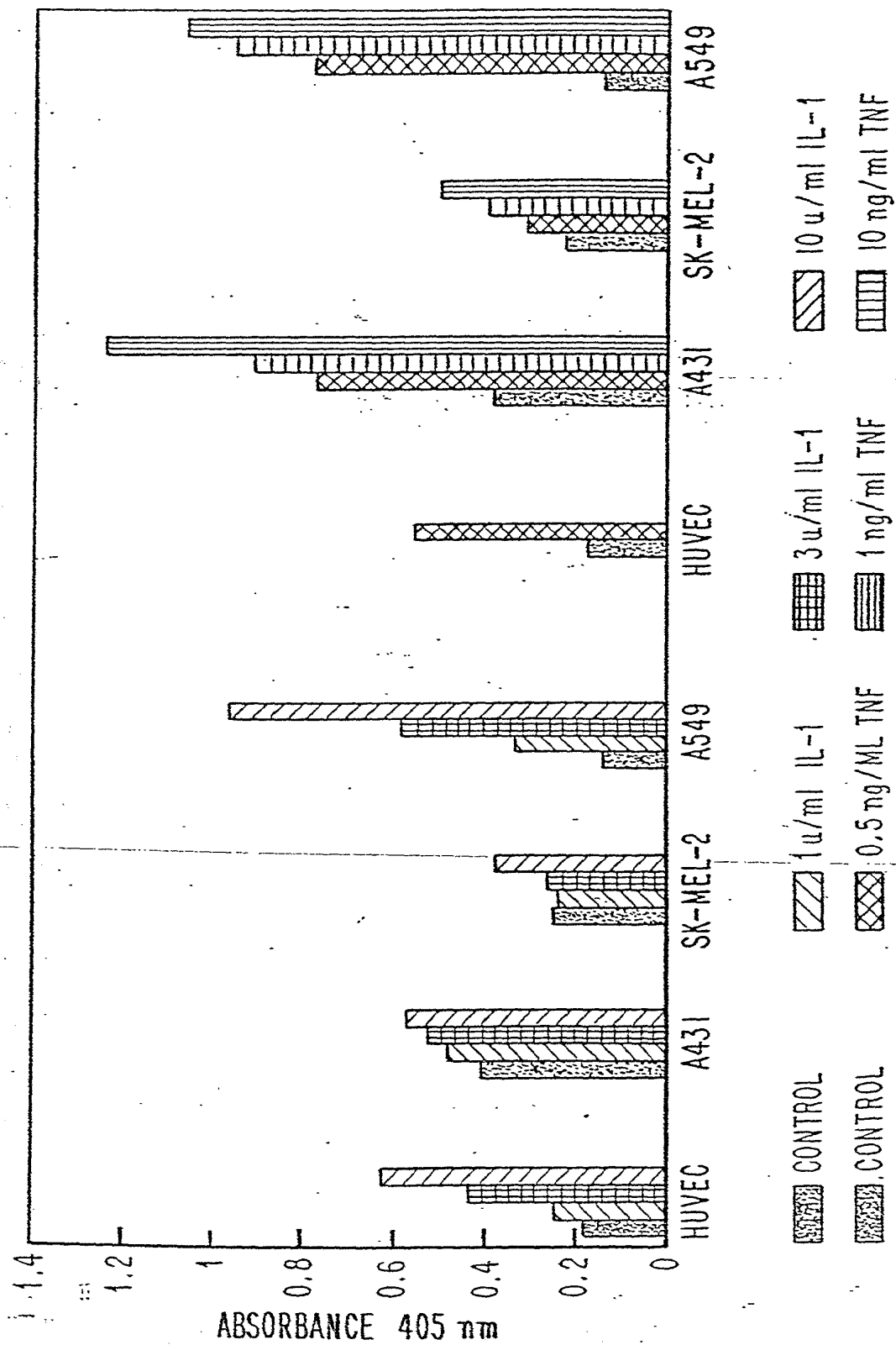


FIG. 4

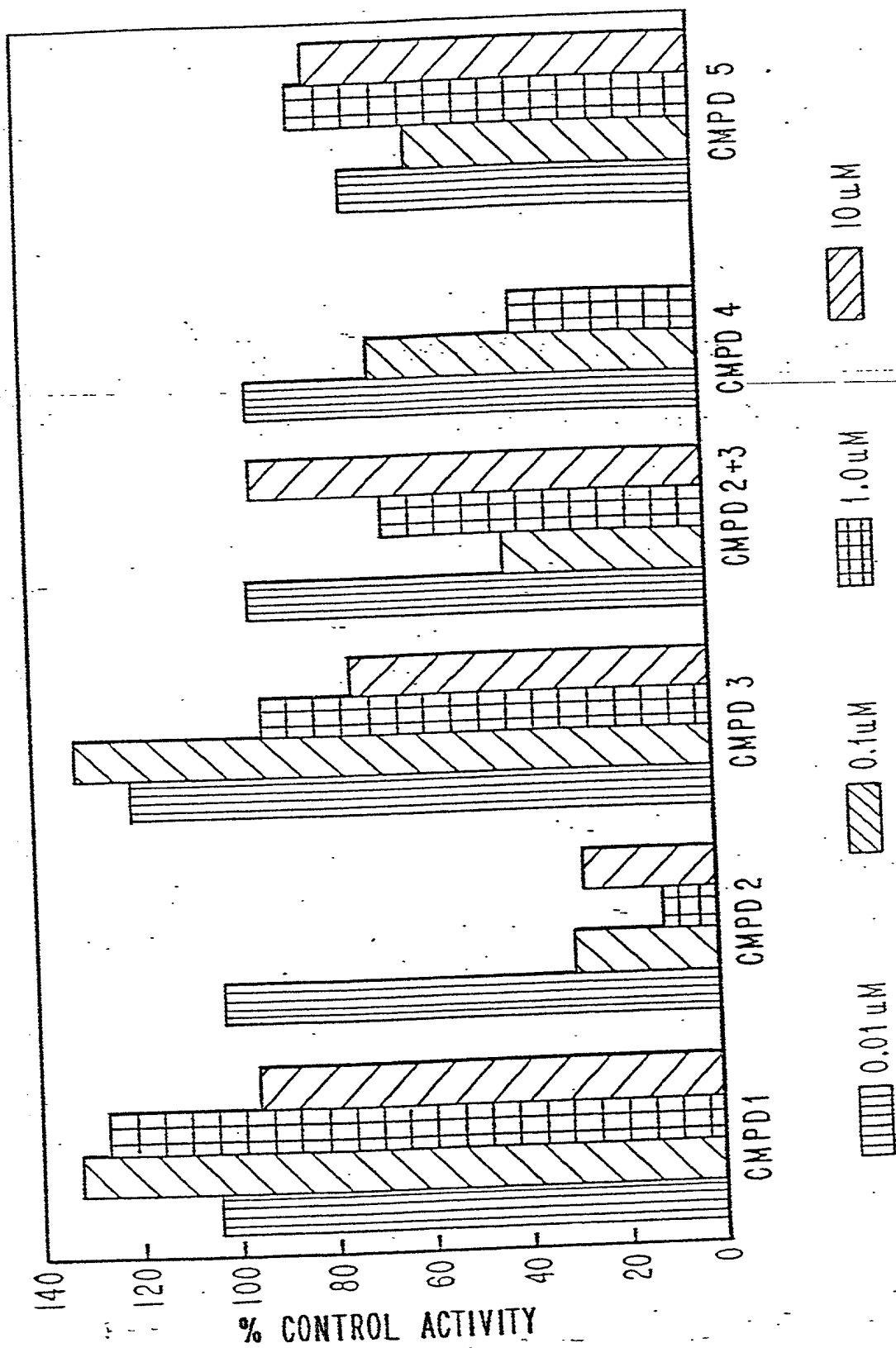


FIG. 5

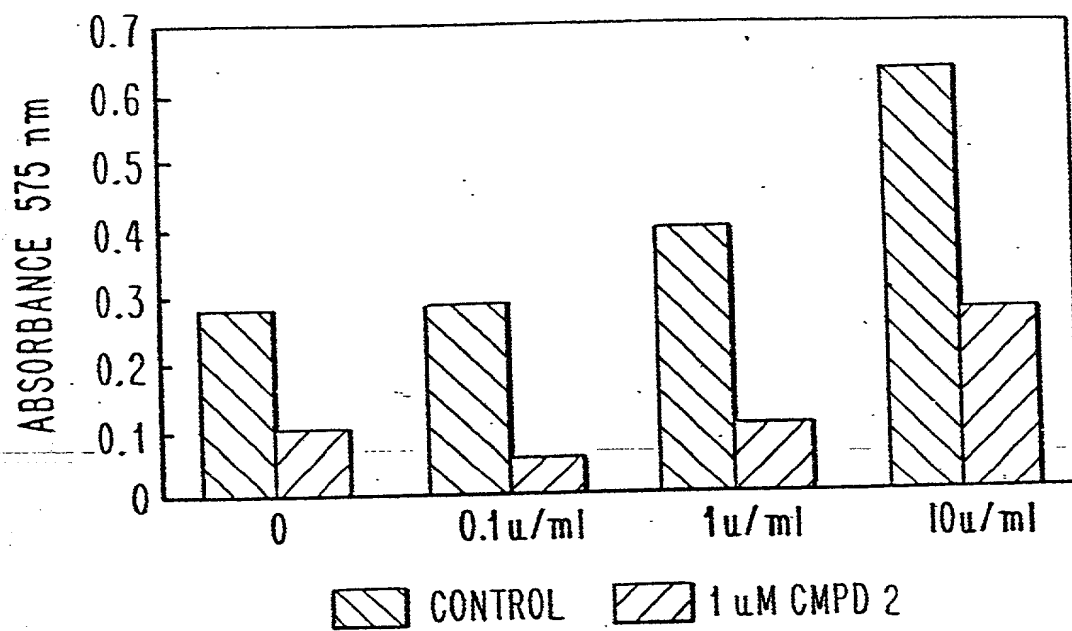


FIG. 6A

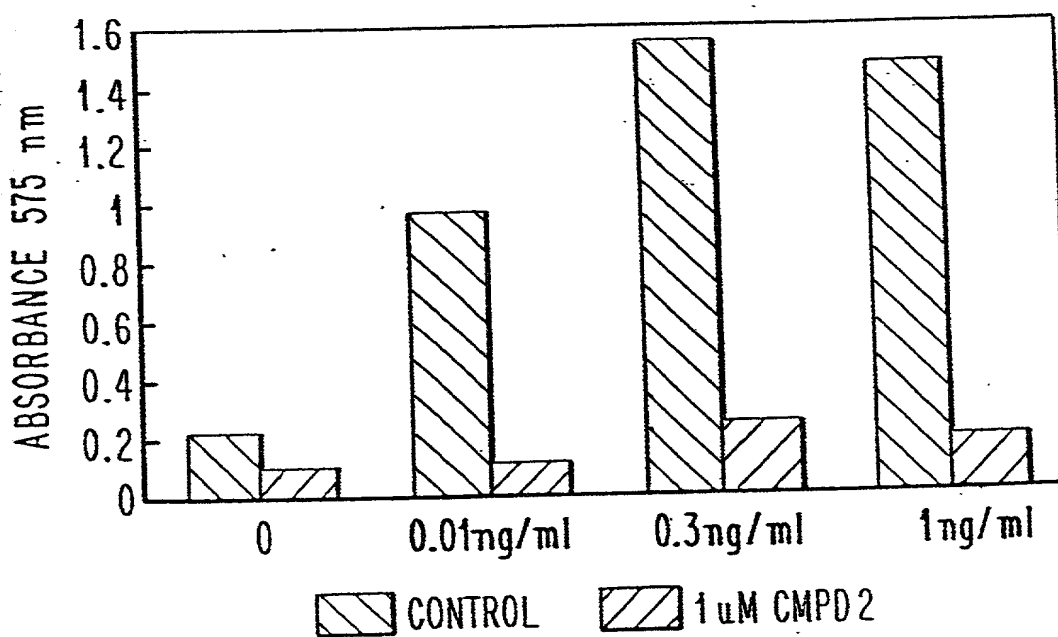


FIG. 6B

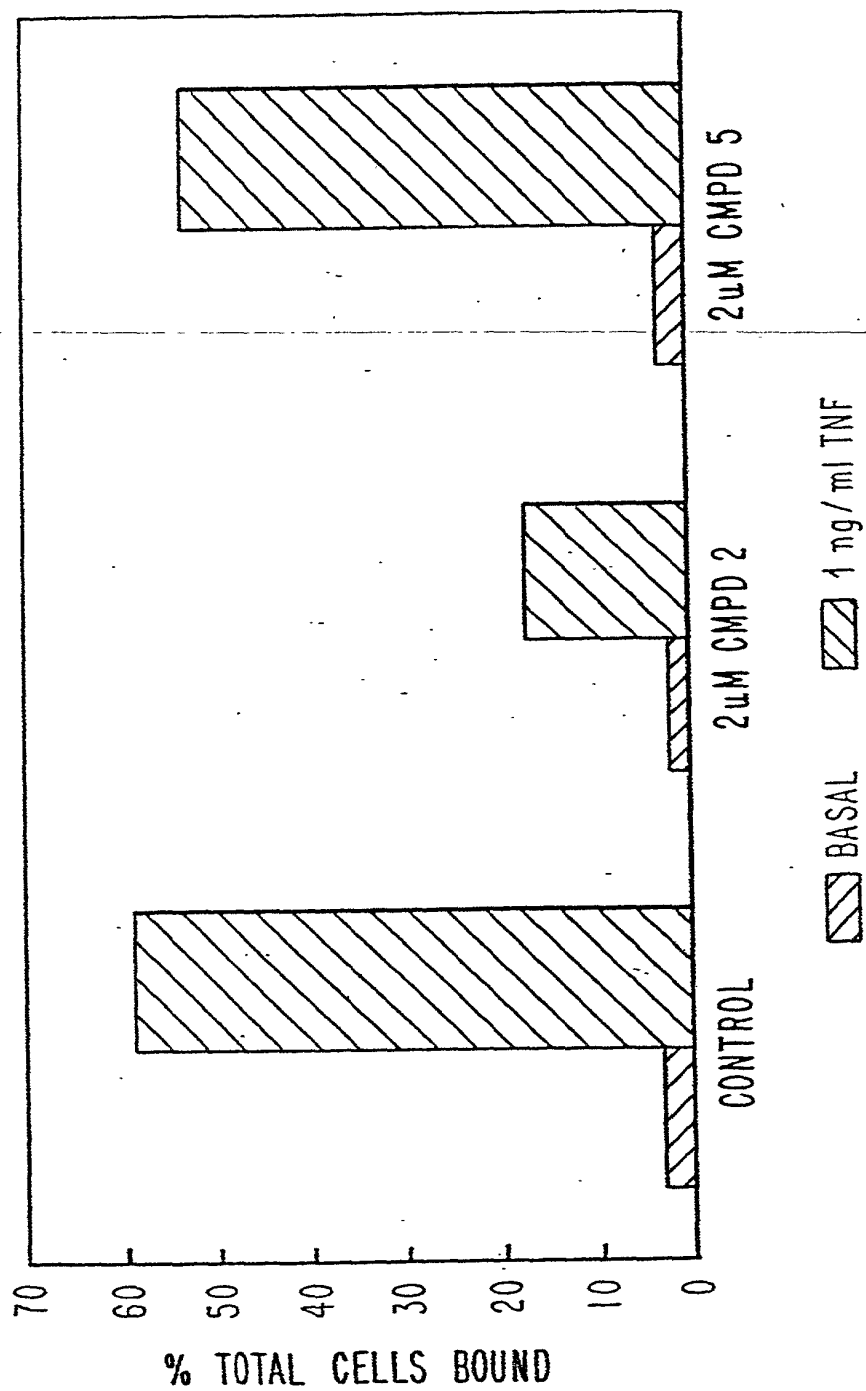
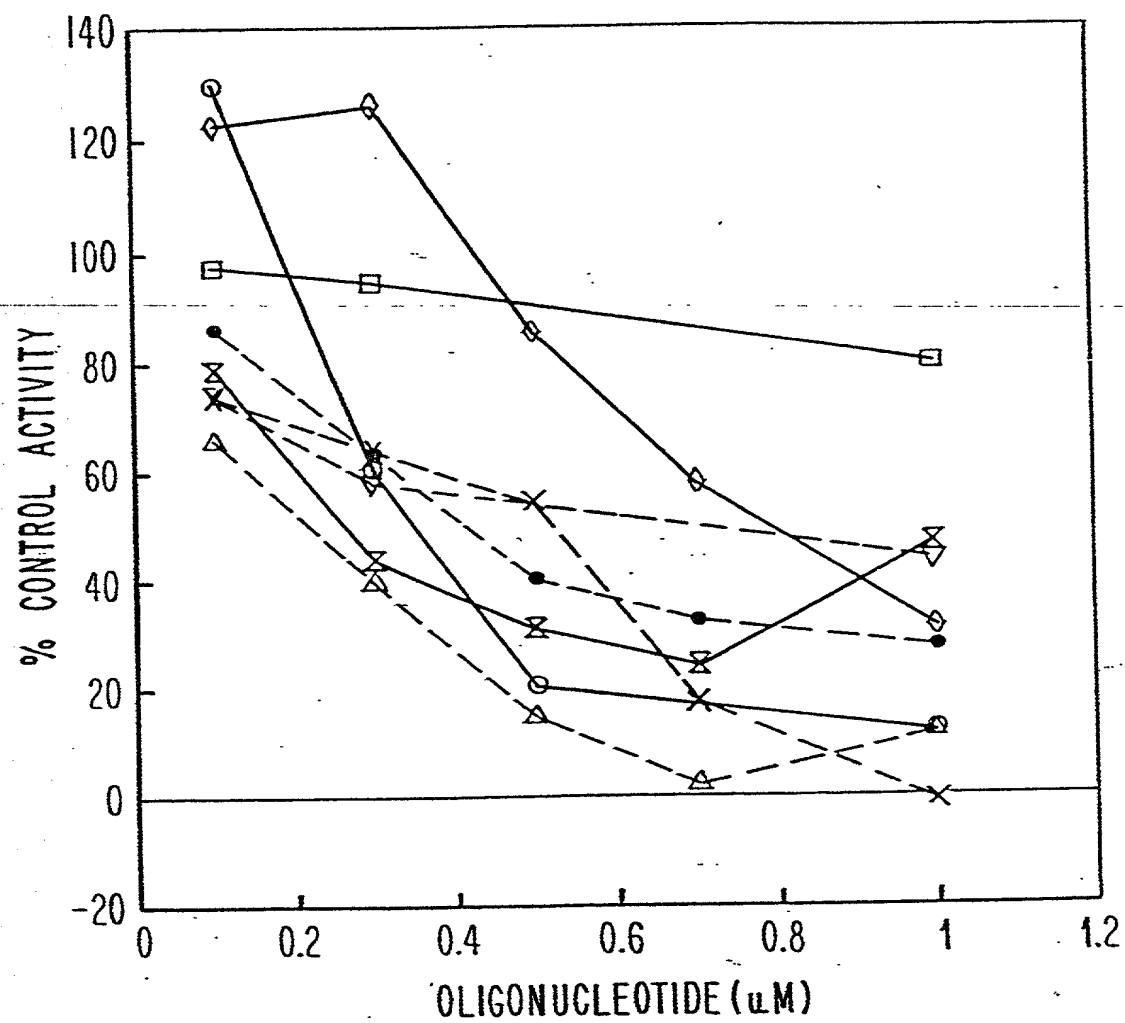


FIG. 7

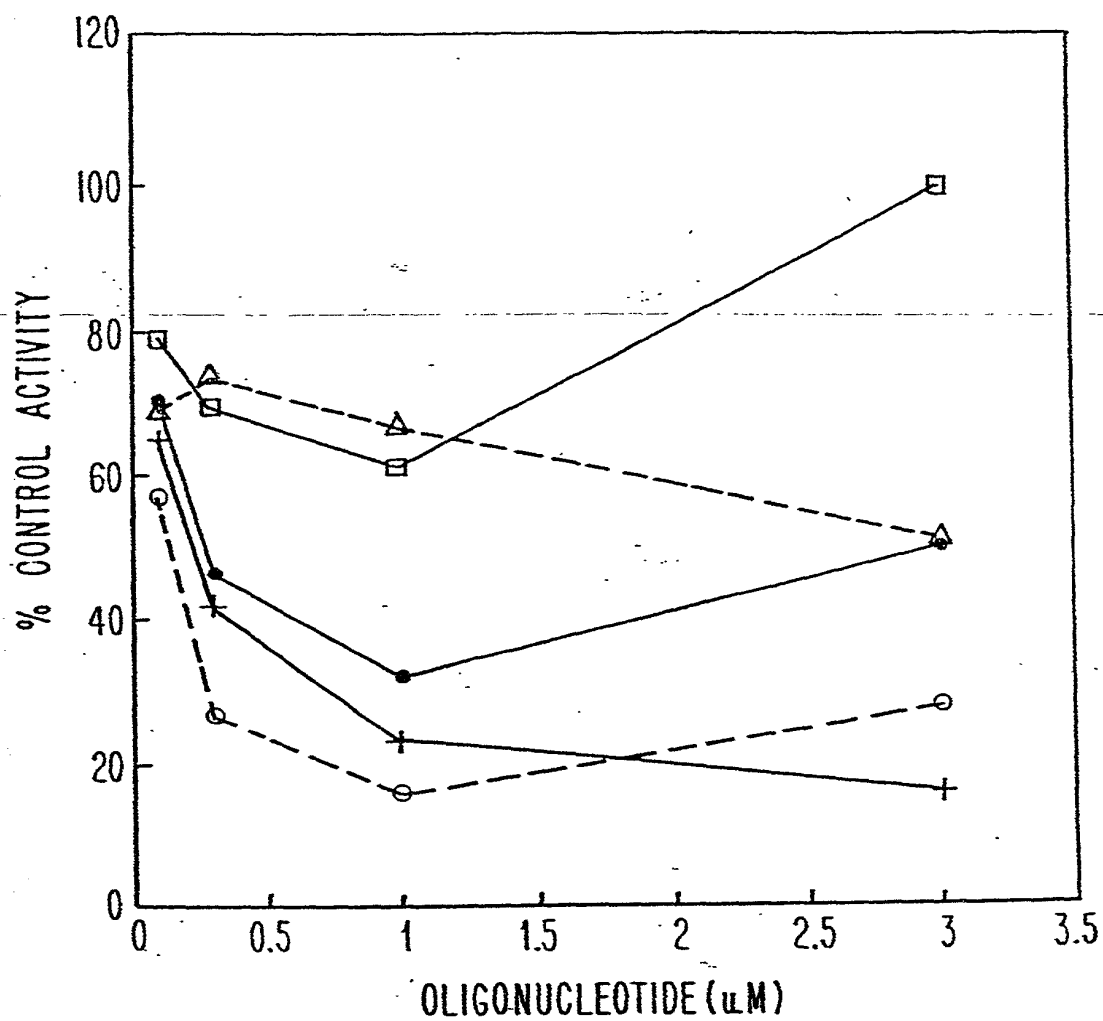
103101-2922860



● 1570	○ 3067	▽ 1931	□ 1932
× 1939	◇ 2307	△ 2302	⊠ 1938

FIG. 8

099226-101841



• 1570

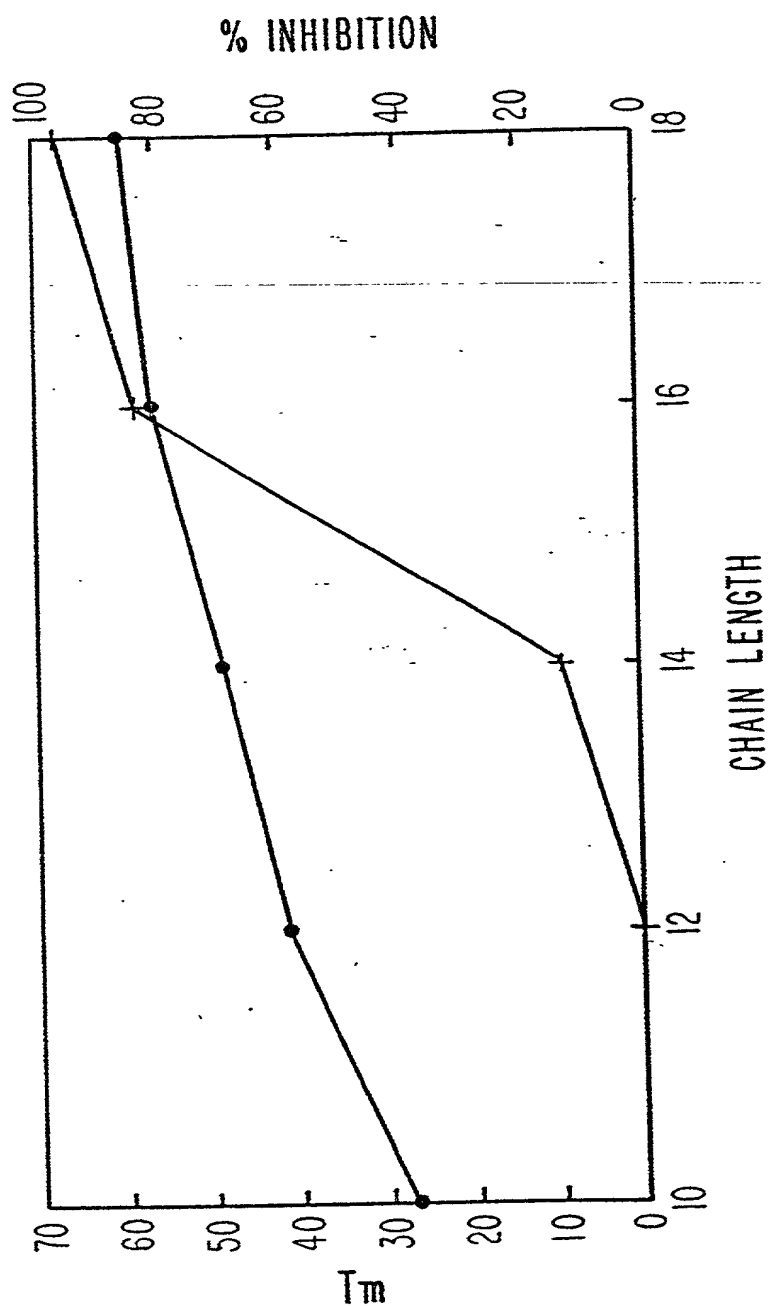
+ 1939

△ 1940

□ 1821

○ 2302

FIG. 9



• T_m + % INHIBITION
100 nM OLIGONUCLEOTIDE

FIG. 10

FIG. 11

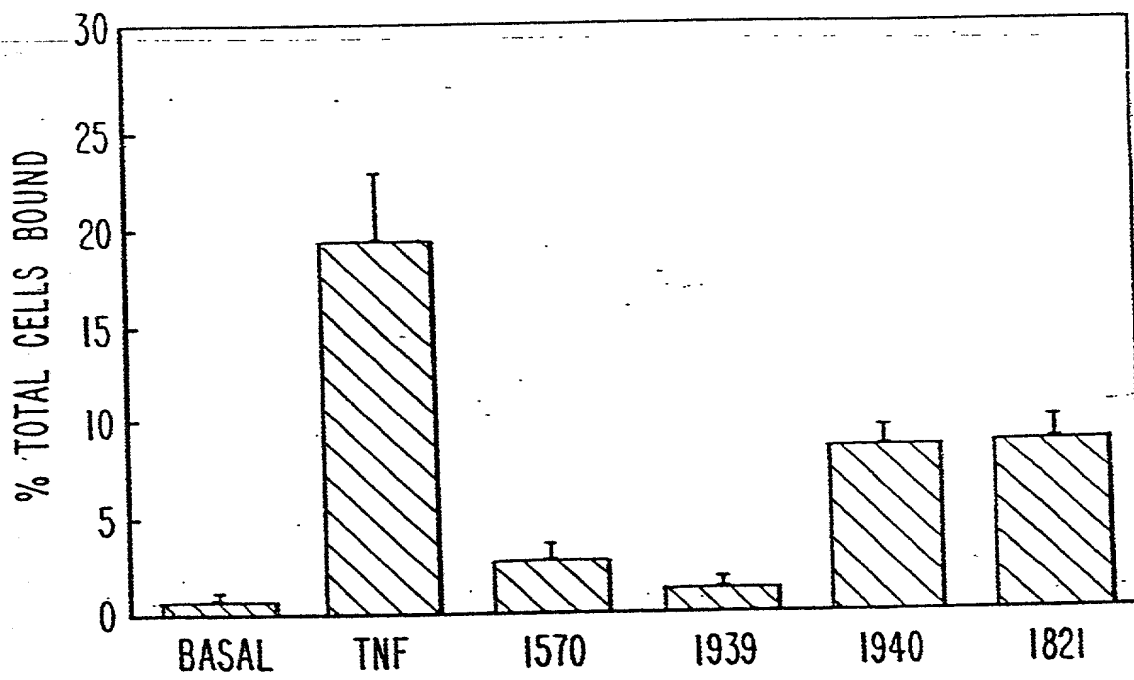


FIG. 11

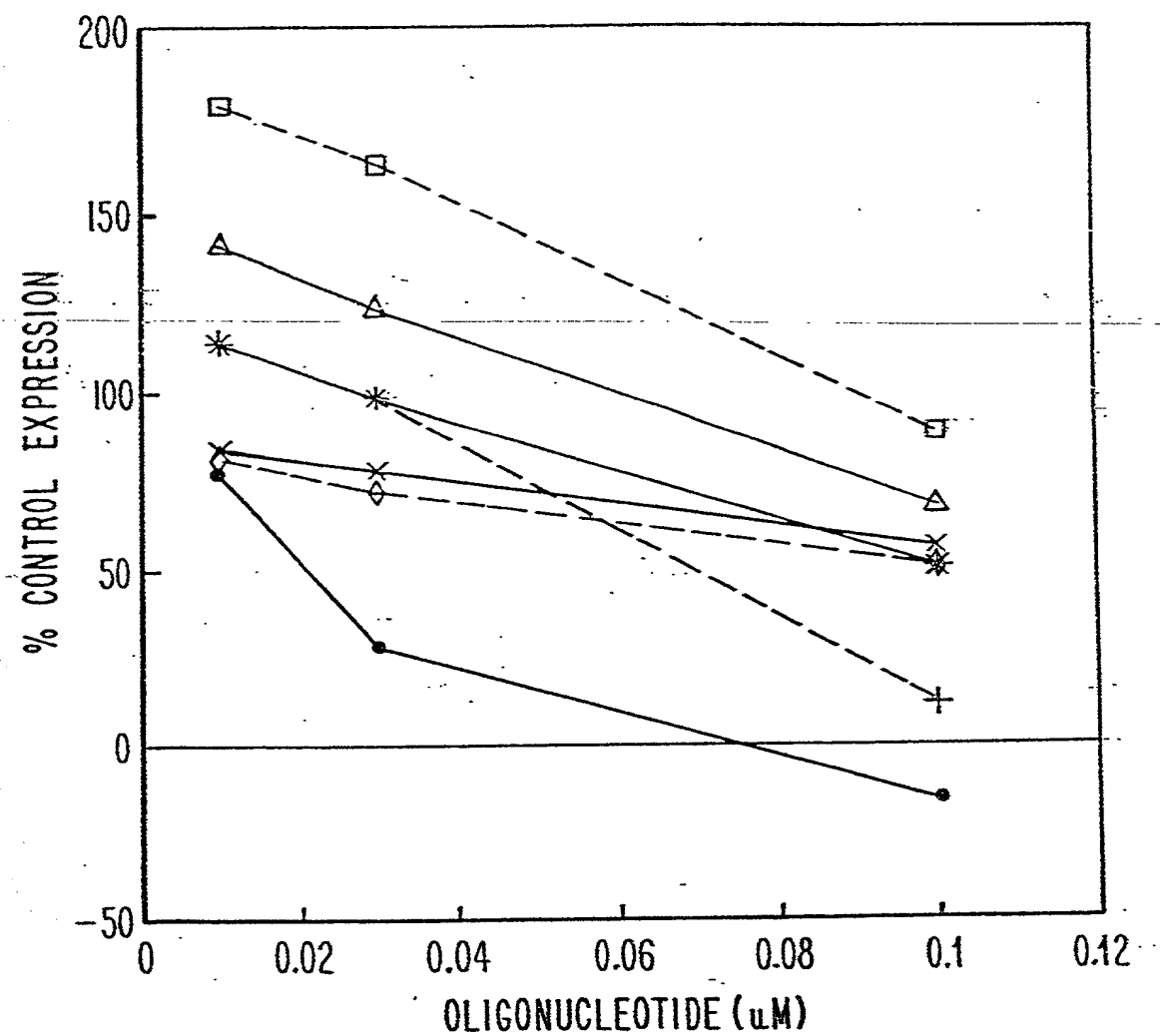


FIG. 12

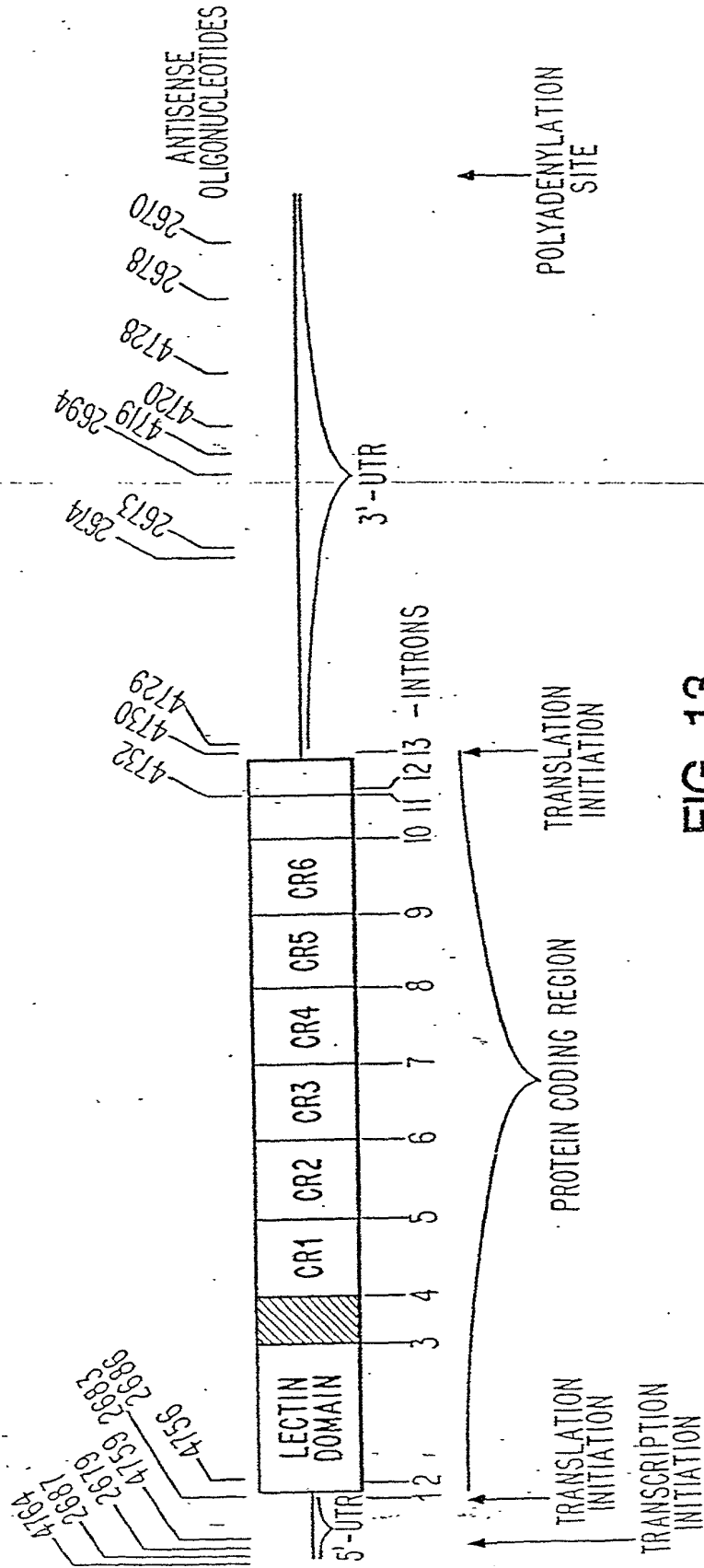


FIG. 13

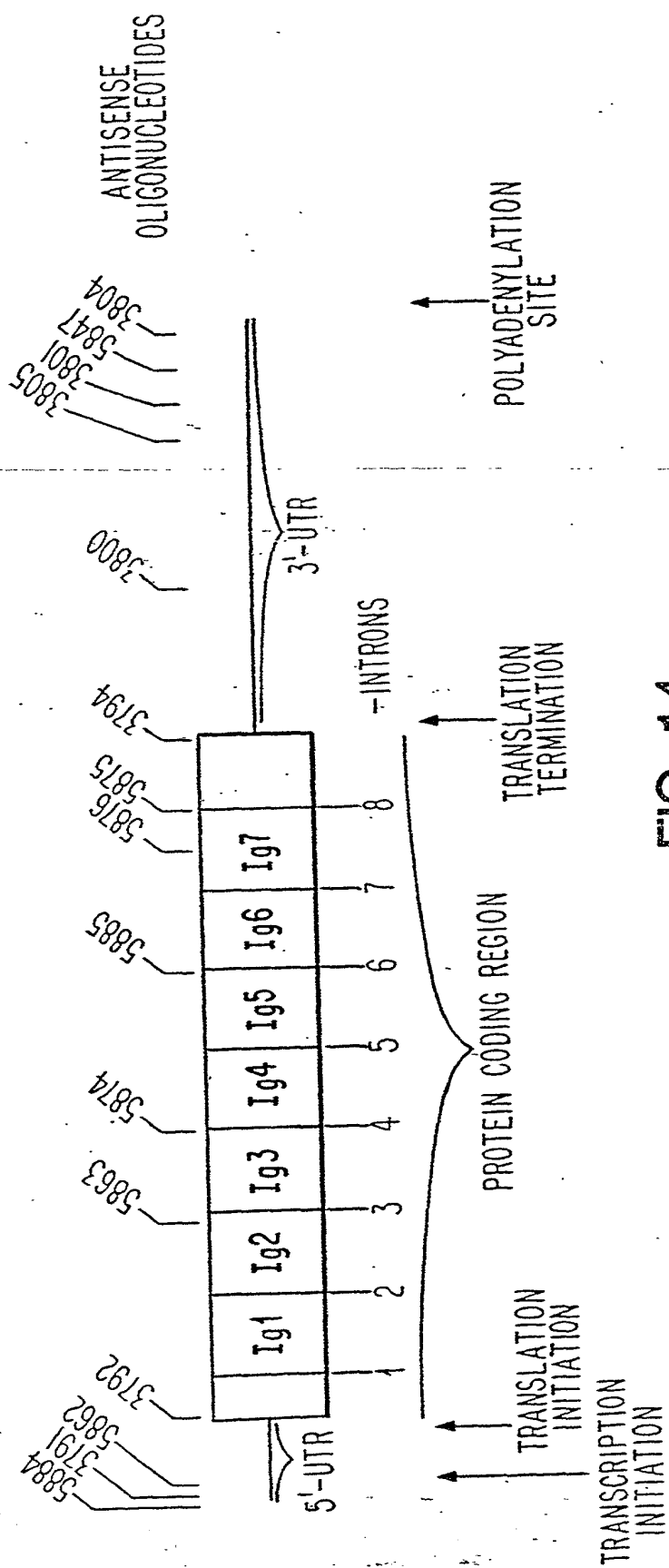


FIG. 14

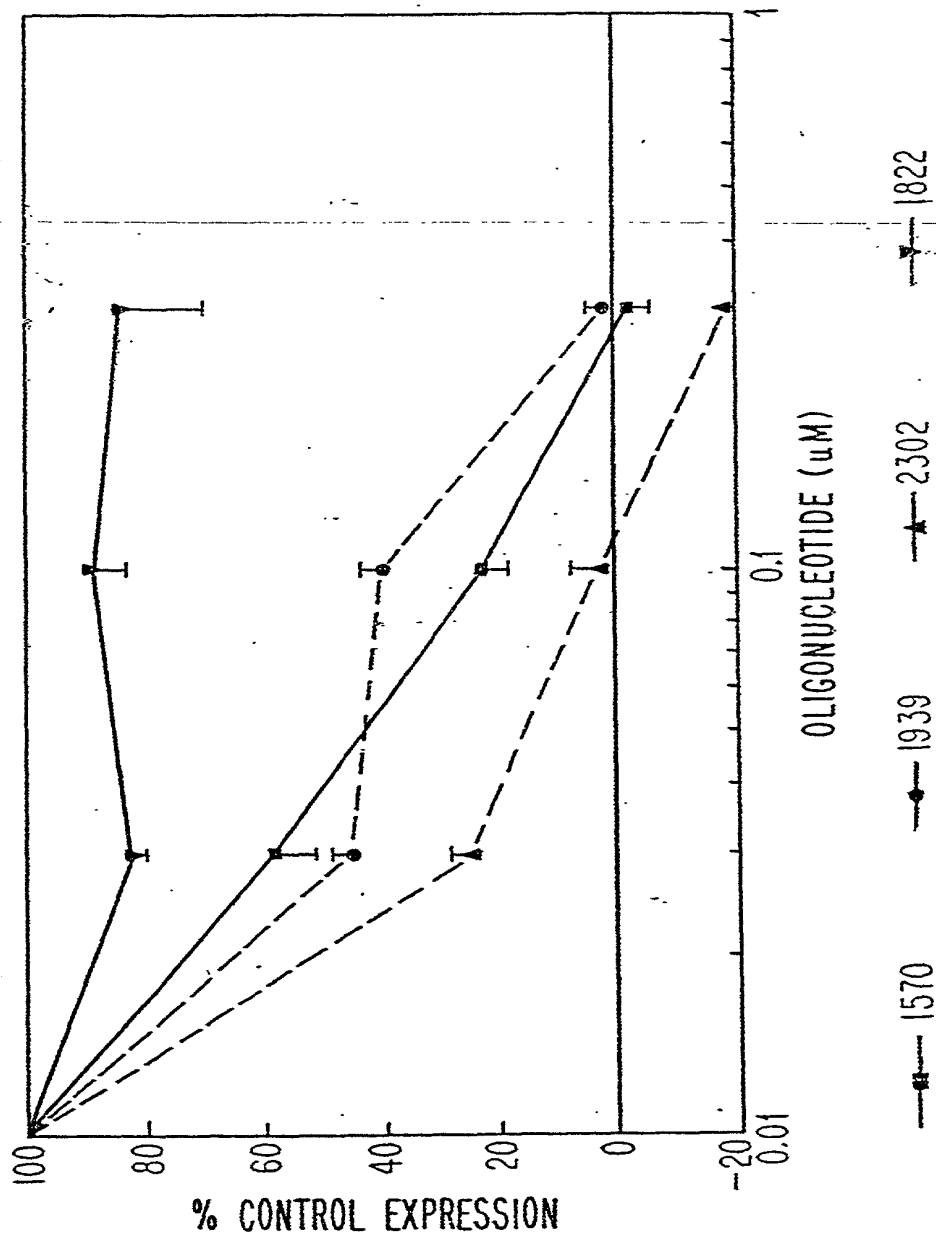


FIG. 15

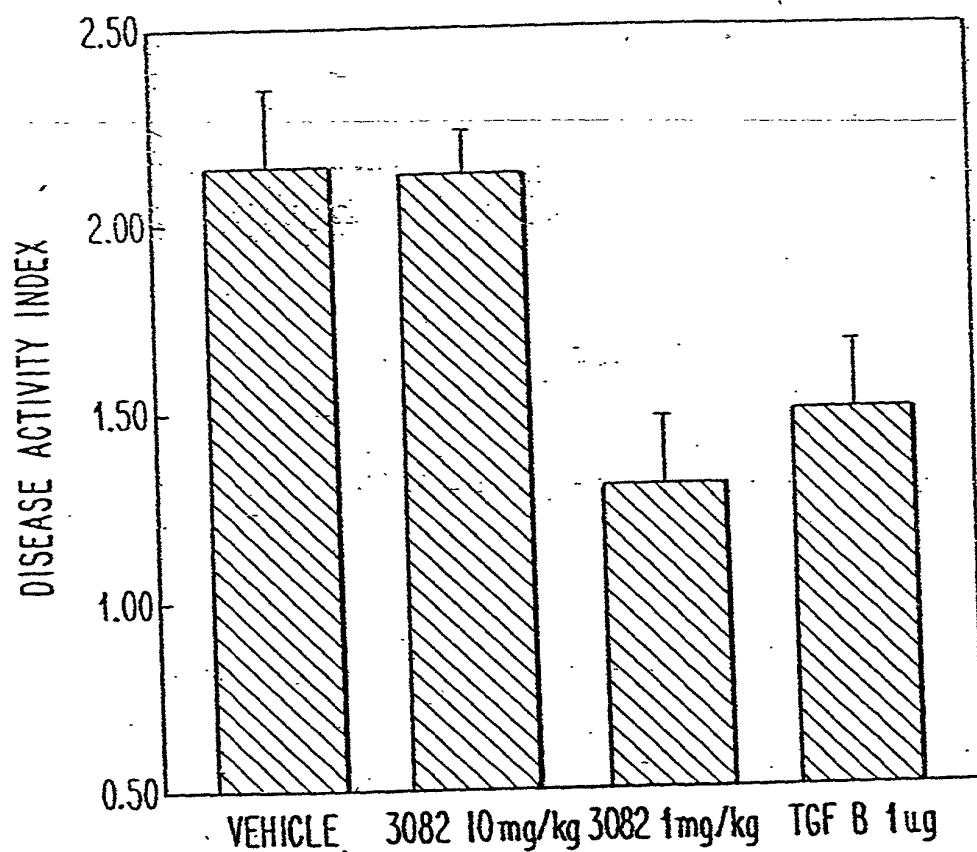


FIG. 16